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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/808,880	03/24/2004	Steven M. Watkins	475512000400	7468

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MORRISON & FOERSTER LLP
755 PAGE MILL RD
PALO ALTO, CA 94304-1018

EXAMINER	
SAUCIER, SANDRA E	
ART UNIT	PAPER NUMBER
1651	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	12/27/2006	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/808,880	WATKINS, STEVEN M.	
	Examiner	Art Unit	
	Sandra Saucier	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 October 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-62* is/are pending in the application.

4a) Of the above claim(s) *3-5,10,15-20,24,25,29,36,38-41,43,50 and 57* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,6-9,11-14,21-23,26-28,30-35,37,42,44-49,51-56 and 58-62* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *24 March 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4/19/04,10/19/06,11/13/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-62 are pending. Claims 1, 2, 6-9, 11-14, 21-23, 26-28, 30-35, 37, 42, 44-49, 51-56, 58-62 are considered on the merits. Claims 3-5, 10, 15-20, 24, 25, 29, 36, 38-41, 43, 50, 57 are withdrawn from consideration as being drawn to a non-elected invention.

Election/Restriction

Claims 3-5, 10, 15-20, 24, 25, 29, 36, 38-41, 43, 50, 57 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b) as being drawn to a non-elected species. Election was made without traverse in Paper No. 10/19/06.

The elected species are directed to a method to determine if a pharmaceutical, nutritional, genetic, toxicological or environmental treatment, regimen or dosage influences *de novo* fatty acid synthesis in liver tissue as determined from the quantitation of palmitoleic or palmitic acid in the cholesterol ester fraction in plasma.

Information Disclosure Statement

The listing of the references on PTO 1449 is incomplete. A proper citation includes AUTHOR, TITLE, JOURNAL, VOLUME, NUMBER, INCLUSIVE PAGES, (month), YEAR. The citation of Siguel is missing the date of publication of the article. Other crossed-out citations are duplicates.

Claim Rejections - 35 USC § 112

SCOPE

Claims 1, 2, 6-9, 11-14, 21-23, 26-28, 30-35, 37, 42, 44-49, 51-56, 58-62 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while perhaps being enabling for assessing *de novo* fatty acid synthesis in adipose tissue by sampling adipose tissue, assessing *de novo* fatty acid synthesis in heart by sampling heart tissue, assessing *de novo* fatty acid synthesis in liver by sampling liver or plasma, does not reasonably provide enablement for assessing *de novo* fatty acid synthesis in a cell, organism or

tissue by sampling any other cell, tissue or any part of an organism and quantifying a marker in the sampled tissue. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to the invention commensurate in scope with these claims.

For example, one would not reasonably assume that *de novo* fatty acid synthesis in the brain could be assessed by sampling heart tissue. Nor would one reasonably expect that *de novo* fatty acid synthesis in a cell or an organisms such as a glial cell could be assessed by sampling adipose tissue, etc. nor does the specification teach such relationships. However, this is the breadth of the independent claim.

The specification does not teach the hypothetical relationships between tissues described above. The specification may teach that *de novo* fatty acid synthesis in the liver at best, may be correlated with markers which are specific fatty acids or classes of fatty acids from specific types of lipids found in the liver or perhaps plasma, *de novo* fatty acid synthesis in the heart may be correlated with markers found in the heart, *de novo* fatty acid synthesis in adipose tissue may be correlated with markers found in the adipose tissue, etc.. However even this is uncertain at the present.

Further, the specification does not teach what markers from which tissue are associated with any condition, for example menopause or auto immune diseases or aging, for example, see page 62 where a list of diseases or conditions are listed. However, no positive correlation of any condition or disease with any fatty acid "marker" appears to be demonstrated.

The exemplification is of mice from which plasma, adipose, liver and heart samples have been substantially completely analyzed for lipid class and types. It appears in Experiment 1 that mice have been administered rosiglitazone and extracts from the tissues analyzed in each lipid class for fatty acid identity and mass? as it is not stated if the quantities are in terms of grams/tissue, moles per ml plasma, moles per gram tissue, etc. However, no

persistent correlation with at least one of applicant's elected species, 16:0, 16:1n7 appears in the cholesterol ester class (elected species) from plasma and *de novo* synthesis in the liver.

The specification, while perhaps describing a methodology of complete lipid type and identity analysis and philosophical hypothetical predictions of usefulness or potential, fails to correlate any of the claimed, broad classifications with a consistent variation in cholesterol ester palmitate or palmitoleate from plasma with *de novo* fatty acid sythesis changes in the liver.

In fact, example 1 demonstrates that administration of the drug, rosiglitazone, decreases the content of palmitate in the ester fraction of cholesterol esters isolated from plasma from 140.4 ± 19.7 to 113.0±4.0, while the content of palmitoleic acid increases from 114.1±12.4 to 200.8± 39.4. In the liver, which is supposed to be the target tissue for *de novo* synthesis predicted by the plasma values, the mass of total fatty acids in the liver in all classes added together appears to increase by a significant amount. The specification fails to teach what the correlation is or even if one exists.

With regard to feeding the drug, CL 316,243 to mice in example 2, the plasma cholesterol palmitate content in the control is 144.8±7.0 and decreases to 114.4± 10.3 in the treated mice, while the 16:ln7 content of plasma cholesterol palmitate is 228.6±23.2 and decreases to 84.9± 31.5 in the treated group. The *de novo* fatty acid synthesis in the liver, at least from an analysis of total fatty acid content, appears to be uneffected. Since experimental mice have tightly controlled diets and should have been paired fed for the experiment since the effect of diet on lipid content of the animal is well known, variation of total fatty acid content from the control to experimental should be some sort of measure of *de novo* synthesis.

In short, the specification fails to show that there is a consistent correlation between *de novo* total fatty acid synthesis in the liver and the palmitic acid or palmitoleic acid content of the cholesterol ester fraction in

plasma (mass or accumulation or concentration) and further fails to show what correlation exists for any disease, condition, genetic, toxicological or environmental treatment, etc..

While the method of completely analyzing all of the lipid metabolites in all the lipid classes in a tissue might be employed to determine specific effects on lipid metabolism in that tissue after administration of a drug, this is not what is being claimed.

The state of the art with regard to a correlation between a weight gain or loss due to a nutritional treatment and a change in a marker of *de novo* fatty acid synthesis in a tissue as in one embodiment of the claimed invention is undeveloped.

With regard to the claims where a method of determining whether a treatment will cause weight gain or loss, weight gain is not only dependent on *de novo* fatty acid synthesis, but also on fatty acid oxidation. See Kusunoki *et al.* [U], "Modulation of Fatty Acid Metabolism as a ***Potential*** Approach to the Treatment of Obesity and the Metabolic Syndrome" (italics are mine).

Nutrition Reviews 1991 [V] states that there is no difference in *de novo* fatty acid synthesis due to non-insulin dependent diabetes, (page 255). Thus, in claim 42, for example, neither the specification nor the state of the art provides a correlation with propensity, risk or metabolic basis for diabetes.

De novo fatty acid synthesis is depressed in animals consuming a high fat diet; however, these animals may gain weight even though *de novo* fatty acid synthesis is depressed. An animal on a low-fat, high carbohydrate diet may have elevated *de novo* synthesis and weight gain, see the review by Parks *et al.* [W]. Thus, *de novo* fatty acid synthesis has not been shown to be correlated with the propensity, risk or metabolic basis for weight gain or loss either by the specification or the state of the art.

Guo *et al.* [X] teach that *de novo* lipogenesis under eucaloric or hypocaloric conditions occurs mainly in the liver, while under hpercaloric conditions adipose tissue is the site of appreciable *de novo* synthesis (discussion).

Thus, no correlation has been taught by either the specification or the prior art between *de novo* fatty acid synthesis as measured by the mass or quantity or concentration of palmitic or palmitoleic acid in plasma to demonstrate *de novo* fatty acid synthesis in the liver with disease or condition or any propensity for success in a treatment.

Undue experimentation would be required to practice the invention as claimed due to the amount of experimentation necessary because of the limited amount of guidance and limited number of working examples in the specification, the nature of the invention, the state of the prior art, breadth of the claims and the unpredictability of the art.

As set forth in In re Fisher, 427 F2.d 833, 839, 166 USPQ 18, 24 (CCPA) 1970: [Section 112] requires that the scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art.

In cases involving unpredictable factors, such as most chemical reactions and physiological activity, the scope of the enablement varies inversely with the degree of unpredictability of the factors involved. Ex parte Humphreys, 24 USPQ2d, 1260.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action: A person shall be entitled to a patent unless (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent, (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 21, 61 and 62 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Volpe *et al.* [IDS].

The claim is directed to a method of assessing *de novo* FA synthesis in a cell, organism, or tissue of the organism comprising:
quantifying a marker of *de novo* fatty acid synthesis in a biological sample from the organisms, wherein the marker is palmitoleic, vaccenic, palmitic, stearic, oleic, myristic, n7 fatty acids, all saturated fatty acids or a combination of any two or more of these and where the marker is measured in a specific lipid category.

Volpe *et al.* disclose the administration of glucocortidcoid to glial cells and the measurement of the *de novo* synthesis of fatty acids in the glial cells, specifically palmitic acid by measuring the activity of fatty acid synthetase.

Claims 1, 2, 6-9, 11, 12, 14, 21-23, 30, 32, 37 and 62 are rejected under 35 U.S.C. 102(a) as being clearly anticipated by Pruzanski *et al.* [U2].

Pruzanski *et al.* measure fatty acid content and type in cholesterol esters from normal and acute-phase HDL (Table 2). 16:0 and 16:1n7 fatty acid quantities are shown in Table 2.

These references are applied to demonstrate that the instant generic claim is not allowable.

Conclusion

Applicant should specifically point out the support for any amendments made to the disclosure, including the claims (MPEP 714.02 and 2163.06). Due to the procedure outlined in MPEP 2163.06 for interpreting claims, it is noted that other art may be applicable under 35 USC 102 or 35 USC 103(a) once the aforementioned issue(s) is/are addressed. Applicants should also keep in mind the elected species when amending claims and in arguments.

Applicant is requested to provide a list of all copending applications that set forth similar subject matter to the present claims. A copy of such copending claims is requested in response to the office action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sandra Saucier whose telephone number is (571) 272-0922. The examiner can normally be reached on Monday, Tuesday, Wednesday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, M. Wityshyn can be reached on (571) 272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Sandra Saucier
Primary Examiner
Art Unit 1651
December 19, 2006